Remarks

Information Disclosure Statement

Enclosed are copies of the PTO-1449 forms filed on November 5, 2003 for the convenience of the Examiner in making these references of record. Copies of the references cited on the PTO-1449 form filed on November 5, 2003 were sent on April 8, 2004.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 15 and 19 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection.

The Legal Standard

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art, without undue experimentation (*See, e.g., Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003; *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343 (CCPA 1976)). As affirmed by the Court in *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d

1400, 1402, 1404 (Fed. Cir.1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.* , 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir.1984). There is no requirement for examples.

Claims 15 and 19 are enabled

A proper analysis of the *Wands* factors shows that claims 15 and 19 satisfy the enablement requirement. The quantity of experimentation necessary to make and use the claimed peptides is **not undue.** It would be routine for one of ordinary skill in the art to prepare any peptide of a length of 9 to 100 amino acids comprising the sequence RMFPNAPYL using chemical synthesis techniques, such as solid phase techniques or recombinant techniques. See page 9, line 24 to page 11, line 10 and page 11, line 19 to page 19, line 14. In addition, peptides having a desired amino acid sequence can be obtained from commercial suppliers. Furthermore, one of skill in the art would know how to formulate pharmaceutical compositions, in particular, vaccines, comprising peptides and proteins as the pharmaceutically effective component.

The claims are not directed to any tumor cell as alleged by the Examiner, but to tumor cells in which HLA-A0201 is expressed and WT-1 is over-expressed. These cells,

and methods for their detection, are described on page 2, line 19 to page 3, line 3; page 3, lines 11-15; page 8, line 26 to page 9, line 7; page 35, lines 12-14 and page 35, lines 19-23. It would be routine for one of skill in the art to test a sample of tumor cells from a patient for HLA-A0201 expression and WT-1 over-expression and then administer the WT-1-derived peptides. Therefore, the claims are clearly enabled for treatment of these cells.

The claimed peptides comprise the amino acid sequence RMFPNAPYL, wherein the peptides are presented by HLA-A0201 on antigen-presenting cells (APCs) by binding to HLA-A0201 on APCs (see page 8, lines 15-24 and Example 1 on page 39). No evidence has been provided by the Examiner that one skilled in the art would not expect these peptides to bind directly to MHC molecules. One of ordinary skill in the art would know that larger peptides may be used since larger peptides are internalized and fragmented by suitable antigen-presenting cells, which present the resulting fragments on MHC molecules at their surface. Therefore, when larger peptides comprising the RMFPNAPYL motif are administered, they are internalized and fragmented to a certain degree by APCs and smaller peptides comprising the sequence RMFPNAPYL are presented by the antigen presenting cells (see page 6, lines 6-24 and page 9, lines 16-22).

The enclosed article (Gaiger et al. *Blood* 96(4): 1480-1489 (2000)) demonstrates that a 23-mer peptide comprising the amino acid sequence RMFPNAPYL (p117-139) is endogenously processed to present the target WT-1 peptide and can trigger WT-1-specific cytotoxic T-lymphocytes when administered to mice; cf. e.g. page 1484, left column, 3rd paragraph. Thus, this article establishes that the claims are enabled.

Enclosed is an article, Mailander et al. *Leukemia* 18: 165-166 (2004), demonstrating *in vivo* efficacy of the claimed vaccines. The results demonstrate that vaccination with a WT-1 peptide of the sequence RMFPNAPYL induced a complete remission in a patient with acute myeloid leukemia. This reference establishes that there is a sufficient level of predictability in the art and shows that undue experimentation is not required to develop a vaccine comprising a peptide containing RMFPNAPYL that is effective against established tumors which over-express WT-1.

It is clear from the specification, the relative skill of those in the art, and the predictability of the art, that one of skill in the art could make and use peptides comprising the RMFPNAPYL motif to elicit the production of cytotoxic lymphocytes for the treatment of HLA-AA0201-positive cells, which aberrantly express WT-1, without undue experimentation.

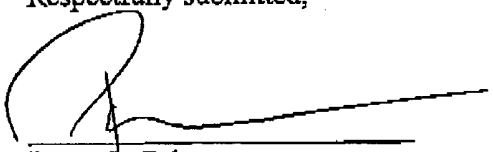
Rejection Under 35 U.S.C. § 102

Claims 1, 5, 7, 15 and 19 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Publication No. 20030082196 by Gaiger et al. ("Gaiger"), which claims priority to U.S. Patent Application No. 09/164,223, ("the '223 application") filed September 30, 1998. Applicants respectfully traverse this rejection.

The claims are limited to HLA-A0201-positive antigen presenting cells (APC) and treatment of HLA-A0201-positive tumor cells, which aberrantly express WT-1. The '223 application does not disclose these limitations nor suggest that the claimed peptides would be processed by HLA-A0201-positive APCs to produce HLA-A0201-bound peptide. Accordingly, the claims are not anticipated by this reference.

Allowance of claims 1, 5, 7, 15, and 19, as amended, is respectfully solicited.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: July 30, 2004

PABST PATENT GROUP, LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151
(404) 879-2160 (fax)